# Investigating Diffusion-MRI based neurite density estimation model dependency: an in-vivo study on the HCP dataset

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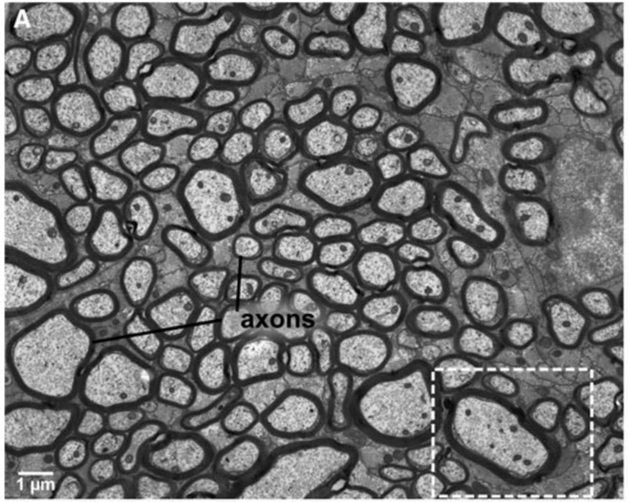
# Neurite Density and Diffusion MRI

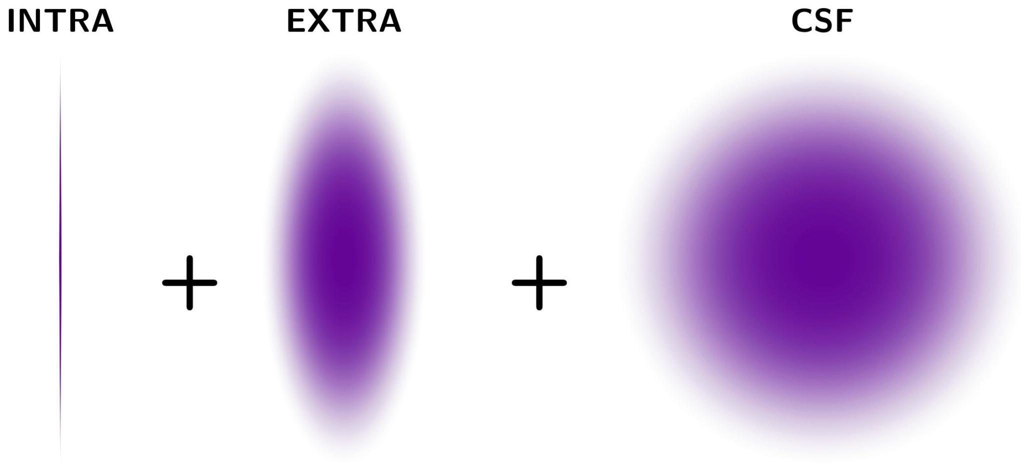
- **Neurite density**[1,2,3,4,5] is one of the most promising microstructural features that can be estimated from **Diffusion-MRI** multi-shell data
- Recent years have seen a proliferation of **Multi-Compartment models** developed to estimate the neurite density




*Nilsson et. al. "The role of tissue microstructure and water exchange in biophysical modelling of diffusion in white matter" Magn Reson Mater Phy (2013) 26:345370*

# Multi-Compartment models

- Multi-Compartment models represents the diffusion signal as a weighted sum of ***compartments***



# Neurite Density and Diffusion MRI

- Neurite density can be calculated from Multi-Compartment models as the **intra-axonal volume fraction** ($\nu_{\mathrm{ia}}$)

$$F(b, \vec{\mathbf{u}}, \vec{\mathbf{v}}) = \nu_{ia} F_{ia}(b, \vec{\mathbf{u}}, \vec{\mathbf{v}}) + \nu_{ea} F_{ea}(b, \vec{\mathbf{u}}, \vec{\mathbf{v}}) + \nu_{csf} F_{csf}(b)$$

- Recent years have seen a **proliferation**[1,2,3,4,5,6,7,9,10] of Multi-Compartment models
- Each of these models makes different **assumptions** about the values of the diffusivity coefficient and the number of compartments

# Spherical Mean Technique

- This MC representation of the diffusion signal is valid only for fibers **aligned** in a single direction
- We can **convolve** the single fiber signal to the *fiber Orientation Distribution Function* (**fODF**)

$$E(b,\vec{\mathbf{u}}) = \int_{\vec{\mathbf{v}}\in\mathcal{S}^2} \rho(\vec{\mathbf{v}}) F(b,\vec{\mathbf{u}},\vec{\mathbf{v}}) d\vec{\mathbf{v}}$$

$$\rho(\vec{\mathbf{v}}) = \sum_{l=0,even}^{\infty} \sum_{m=-l}^{l} c_{lm} Y_l^m(\vec{\mathbf{v}})$$

$$\longrightarrow$$

$$K_l(b) Y_l^m(\vec{\mathbf{u}}) = \int_{\vec{\mathbf{v}}\in\mathcal{S}^2} F(b,\vec{\mathbf{u}},\vec{\mathbf{v}}) Y_l^m(\vec{\mathbf{v}}) d\vec{\mathbf{v}}$$

$$E(b,\vec{\mathbf{u}}) = \sum_{l=0,even}^{\infty} \sum_{m=-l}^{l} c_{lm} K_l(b) Y_l^m(\vec{\mathbf{u}})$$

- With $Y_l^m(\mathbf{v})$ are the real **Spherical Harmonics** (SH) functions

# Spherical Mean Technique

$$E(b,\vec{\mathbf{u}}) = \sum_{l=0,even}^{\infty} \sum_{m=-l}^{l} c_{lm} K_l(b) Y_l^m(\vec{\mathbf{u}})$$

$$\begin{aligned}\overline{E}(b) &= \frac{1}{4\pi} \int_{\vec{\mathbf{u}} \in \mathcal{S}^2} E(b,\vec{\mathbf{u}}) d\vec{\mathbf{u}} \\ &= \frac{1}{4\pi} K_0(b)\end{aligned}$$

- The **mean** of the signal depends **only** on the **microstructural kernel** and not on the **fiber orientation**[7,9,10]

# Aims

In this work:

- We will compare the neurite density estimated using **three** different Multi-Compartment models
- We evaluate its **inter-subject reproducibility**
- We evaluate the effect of the other model **parameters** on its estimation in-vivo

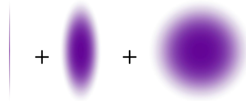
# Multi-Compartment models

**NODDI-SH**

$$E(\mathbf{b}) = (1-\nu_{csf})(E_{ia}(\mathbf{b}, \lambda_{\|}^{ia}) + \nu_{ea}E_{ea}(\mathbf{b}, \lambda_{\|}^{ea}, \lambda_{\perp}^{ea})) + \nu_{csf}E_{csf}(b)$$

$$\lambda_{\|}^{ia} = \lambda_{\|}^{ea} = 1.7 \cdot 10^{-3}\ \mathrm{mm}^2/\mathrm{s}$$

$$\lambda_{\perp}^{ea} = \lambda_{\|}^{ea}\frac{\nu_{ea}}{\nu_{ia}+\nu_{ea}}$$

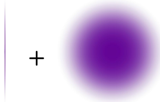


**BS-SH**

$$E(\mathbf{b}) = \nu_{ia}E_{ia}(\mathbf{b}, \lambda_{\|}^{ia}) + \nu_{ea}E_{ea}(\mathbf{b}, \lambda_{\|}^{ea}, \lambda_{\perp}^{ea})$$

$$\lambda_{\|}^{ia} = 1.7 \cdot 10^{-3}\ \mathrm{mm}^2/\mathrm{s}$$

$$\lambda_{\|}^{ea} = \lambda_{\perp}^{ea}$$

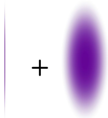


**MC-MDI**

$$E(\mathbf{b}) = \nu_{ia}E_{ia}(\mathbf{b}, \lambda_{\|}^{ia}) + \nu_{ea}E_{ea}(\mathbf{b}, \lambda_{\|}^{ea}, \lambda_{\perp}^{ea})$$

$$\lambda_{\|}^{ia} = \lambda_{\|}^{ea}$$

$$\lambda_{\perp}^{ea} = \lambda_{\|}^{ea}(1-\nu_{ia})$$



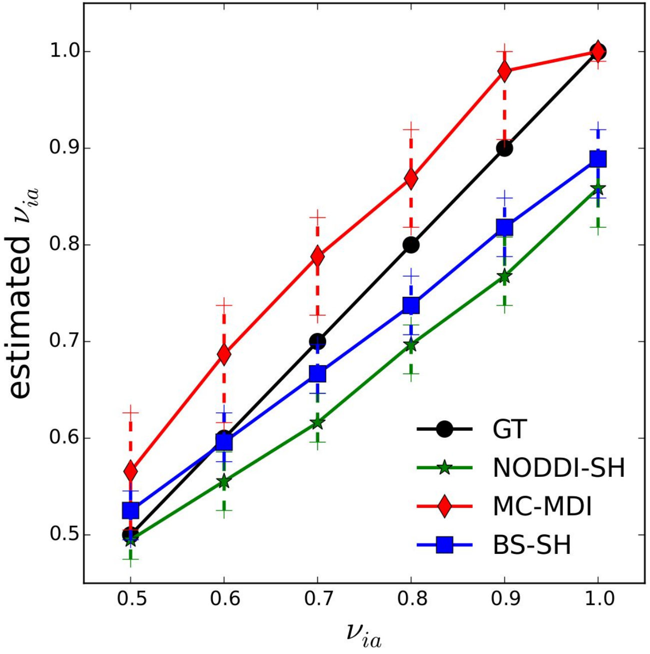
# Human Connectome Project (HCP)

- We considered 10 subjects of the **Human Connectome Project**[8]
- b-values = [1000, 2000, 3000] s/mm$^2$
- 90 gradients per shell plus 18 b 0
- $\Delta$ = 43.1ms and $\delta$ = 10.6ms

# Synthetic data Results (from MICCAI 2017)

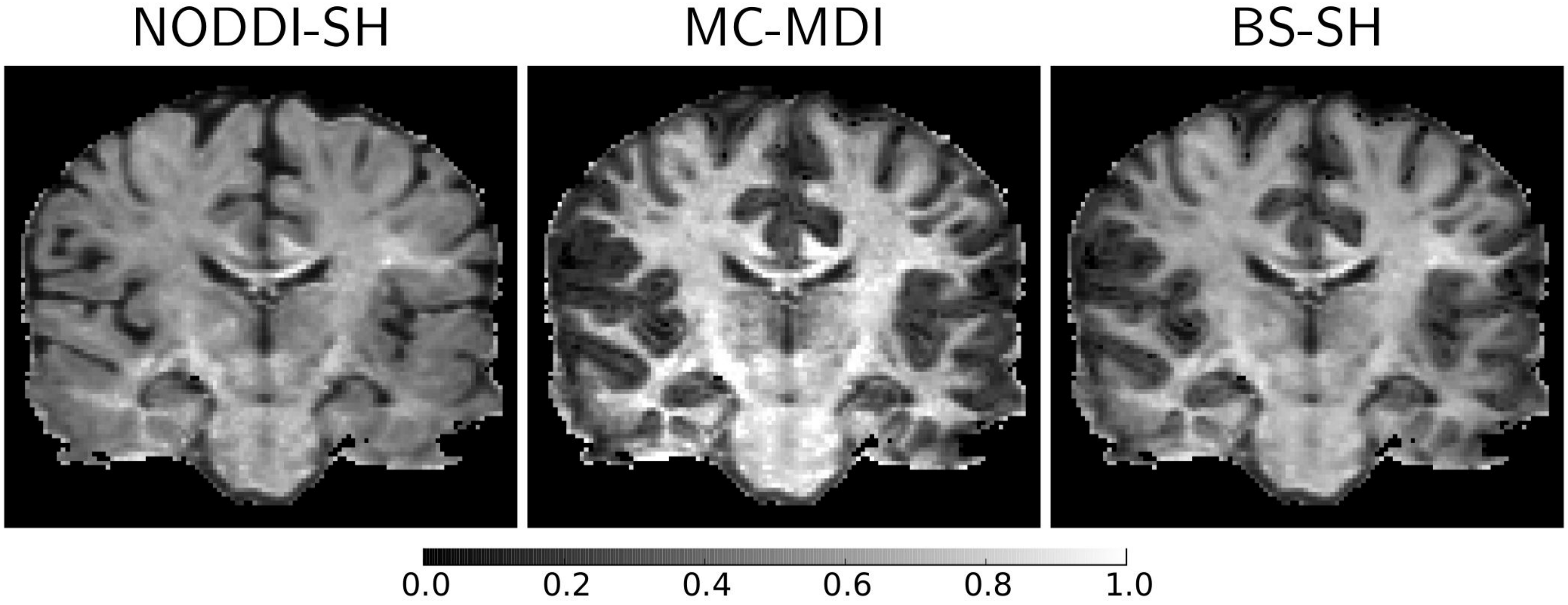
Our previous results[7] on **synthetic data** shown that:

- NODDI-SH and BS-SH tend to **underestimate** the neurite density
- MC-MDI tends to **overestimate** it

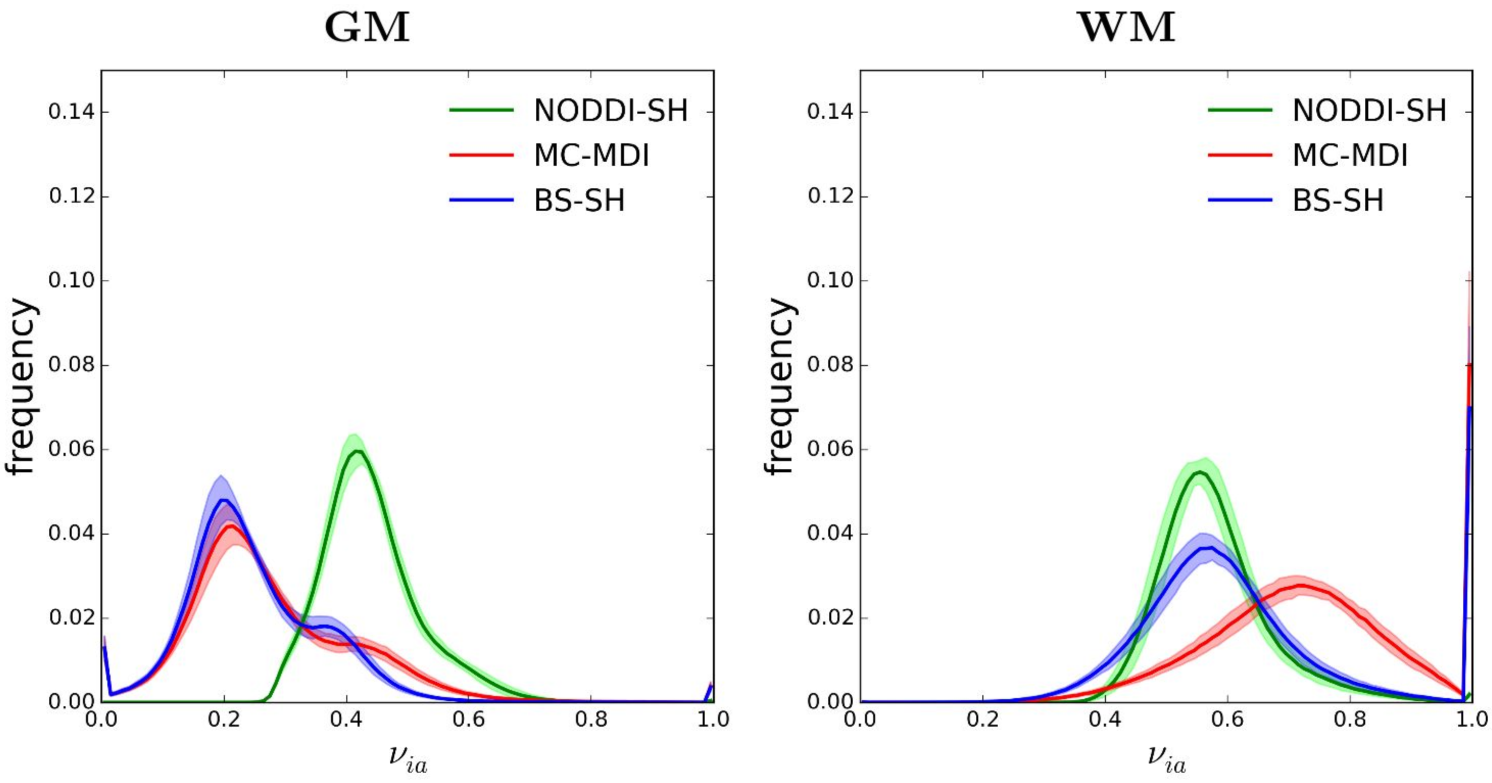



*Zucchelli, M., Descoteaux, M., Menegaz, G. (2017). Proceedings of MICCAI, Workshop on Computational Diffusion MRI (CDMRI)", Canada.*

# HCP Results



# HCP Results



GM
WM
NODDI-SH
MC-MDI
BS-SH
frequency
$\nu_{ia}$
0.00
0.02
0.04
0.06
0.08
0.10
0.12
0.14
0.0
0.2
0.4
0.6
0.8
1.0

# Conclusions

- **Neurite density** has a well defined numerical range and it is **stable** across healthy subjects
- However, its values strongly depend on the **choice of the model** used to calculate it
- Our results suggest that it could potentially be used as a **feature** to discriminate between healthy brains and pathological conditions
- However, it is extremely important to keep in mind that its values are only proportional to the **real underlying neural density** and to compare it only with studies that use exactly the same model for its estimation

# Aknowledgements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- *Data were provided by the Human Connectome Project, WU-Minn Consortium(Principal Investigators: David Van Essen and Kamil Ugurbil; 1U54MH091657)funded by the 16 NIH Institutes and Centers that support the NIH Blueprint forNeuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University.*

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